Dissertation on

"COMPARISON OF GRANISETRON WITH THE COMBINATION OF GRANISETRON AND DEXAMETHASONE IN THE PROPHYLAXIS OF POST OPERATIVE NAUSEA AND VOMITING"

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CERTIFICATE

This is to certify that the dissertation **"COMPARISON OF GRANISETRON WITH THE COMBINATION OF GRANISETRON AND DEXAMETHASONE IN THE PROPHYLAXIS OF POST OPERATIVE NAUSEA AND VOMITING "** presented herein by **Dr.P. JOTHI ANAND,** is an original work done in the Department of Anesthesiology, Government Stanley Medical College and Hospital, Chennai, in partial fulfillment of regulations of the Tamilnadu Dr.M.G.R.Medical University for the award of degree of M.D. (Anesthesiology) Branch X, under my guidance and supervision during the academic period 2005-2007.

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DECLARATION

I **Dr.P. JOTHI ANAND.** solemnly declare that this dissertation, titled **"COMPARISON OF GRANISETRON WITH THE COMBINATION OF GRANISETRON AND DEXAMETHASONE IN THE PROPHYLAXIS OF POST OPERATIVE NAUSEA AND VOMITING"** is a bonafied record of work done by me in the Department of Anesthesiology, Stanley Medical College and Hospital, Chennai, under the guidance of **Prof. R. Meenakshi, M.D., D.A.,** Professor and H.O.D., Department of Anesthesiology, Government Stanley Medical College & Hospital, Chennai - 600 001.

This dissertation is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the University regulations for the award of degree of M.D. (Anesthesiology), Branch X, examination to be held in February 2007.

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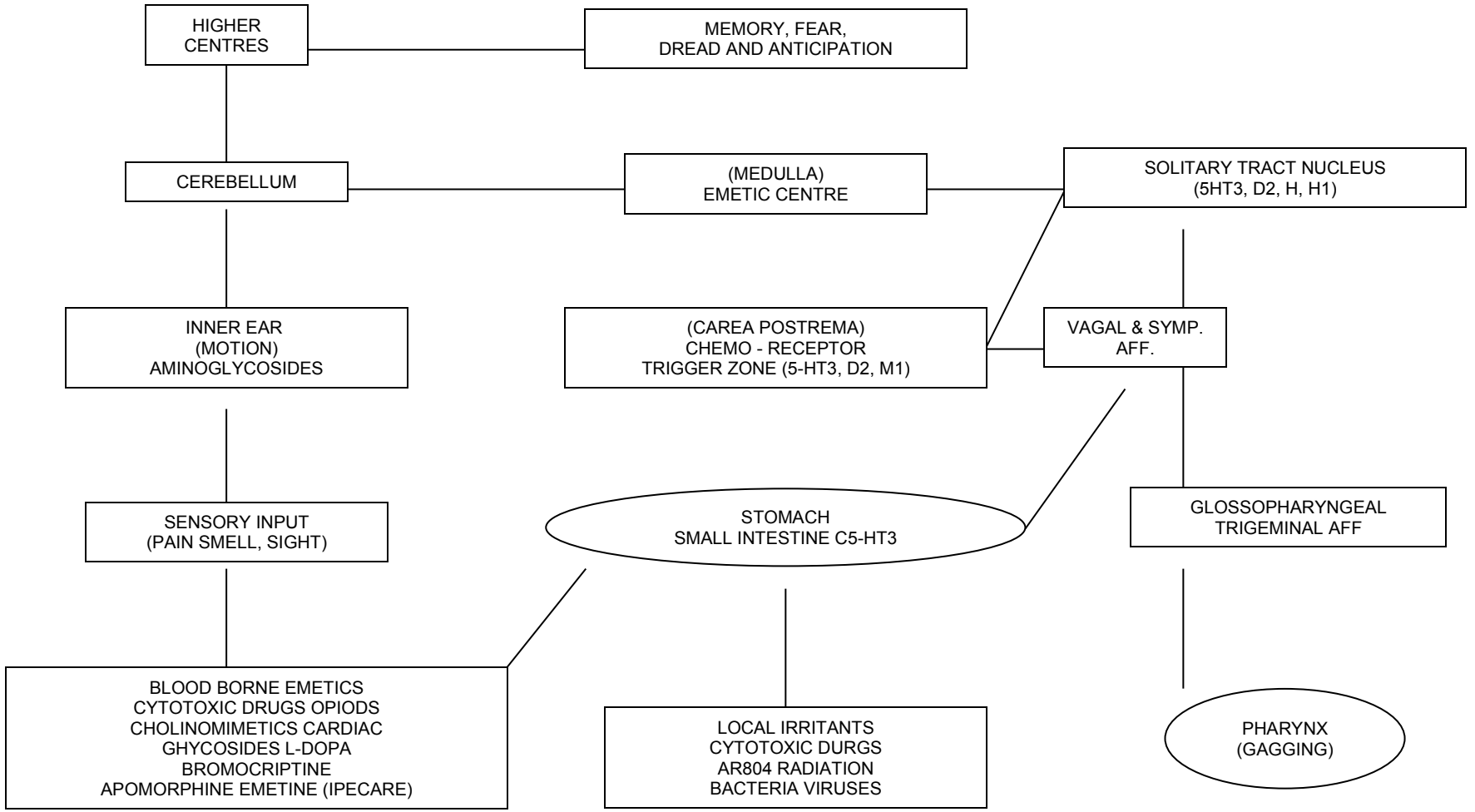
I. INTRODUCTION

Post Operative Nausea and Vomiting (PONV), despite the advance in anaesthetic care, is still a 'big little problem'[1] within the anaesthesia world.[1] It is defined as nausea and/or vomiting that occurs within 24hrs after surgery and can occur following general, regional or local anaesthesia. It is their most distressing concern in post operative period. The incidence can be as high as 80% following certain procedures like ENT, Laparoscopic (or) gynecological surgeries. When severe, post operative nausea and vomiting can lead to wound dehiscence, bleeding, dehydration, electrolyte imbalance, delayed discharge and increased treatment cost.

II AIM OF STUDY

The aim of this study is to compare and evaluate the effect of granisetron and combination of granisetron with Dexamethasone given prophylactically in the prevention of post operative nausea and vomiting in patients undergoing elective ENT surgeries.

PHARAMACOLOGISTS VIEW OF EMETIC STIMULI



III. PHYSIOLOGY OF NAUSEA AND VOMITING

Nausea and vomiting are important defense mechanisms against the ingestion of toxins.

Nausea: It is a subjective sensation of the desire to vomit, but without any attempt at expulsive movements.

Retching: Is the spasmodic, rhythmic contractions of the respiratory muscles including the diaphragm, chest wall and abdominal muscles with out actual expulsion of gastric contents.

Vomiting is the forceful expulsion of gastric contents by strong & sustained contractions of Abdominal muscles.

Mediators Of Vomiting Reflex:

Vomiting is initiated by an afferent pathway stimulus either from viscera (or) from certain areas of brain. These impulses are transmitted by afferent fibers of both the sympathetic and para sympathetic system to the specialized centers in brain, where by an emetic response is initiated.

AFFERENT PATHWAY

1. Chemoreceptor Trigger Zone (CTZ) :

The CTZ is located in the area postrema on the floor of IV ventricle near the vomiting centre. These area is lack of blood brain

barrier and hence responds to circulating drugs like Opoids, Cytotoxic drugs, Cardiac Glycosides, Emetine, transmitters like Dopamine (D_2) 5HT ($5HT_3$) Histamine hormones.

2. Higher Cortical Centre:

Various Psychic stimuli like bad odours, unpleasant sight, pain and fear through various pathway centers stimulate the vomiting centre.

3. Vestibular apparatus:

It sends signal to the vomiting centre through vestibular portion of VIII cranial nerve when it is stimulated either by body movement or by ototoxic drugs.

4. Visceral Receptors

a. Mechano receptors:

Found in the muscle layer of GIT. They are stimulated by distension, contraction of GIT or by physical damage (Surgical stimulus)

b. Chemo receptors:

They are located in the upper GI and respond to irritant which release 5HT from ECF cells. Both these receptors send signals through the vagus and sympathetic afferents via the spinal cord.

5. Glossopharyngeal stimulation is by stimulating the back of the throat, sends signal to vomiting centre.

6. Afferents from renal pelvis, peritoneum and genitalia are relayed by ANS afferent neurons to vomiting centre.

CENTRAL INTEGRATIVE MECHANISM:

Vomiting centre is an ill defined area located in the paracellular area of the lateral reticular formation of medulla in close proximity to the nucleus of tractus solitarius and area postrema at the level of dorsal motor nucleus of the vagus nerve. Vomiting occurs due to stimulation of vomiting centre.

EFFERENT PATHWAY:

The motor impulses that cause actual vomiting are transmitted from vomiting centre through 5^{th}, 7^{th}, 9^{th}, 10^{th} and 12^{th} cranial nerve to the upper GIT and through the spinal nerves to the diaphragm and abdominal muscles.

The act of emesis involves a sequence of events that can be divide into (i) pre ejection. (ii) ejection and (iii) post ejection phases.

The pre ejection phase comprises pro dromal symptoms of nausea, along with autonomic signs such as salivation, sweating, pallor and tachycardia. The ejection phase consist of vomiting and retching. The post ejection phase consist of autonomic and visceral responses that return the body to a quiescent phase with or without residual nausea.

AETIOLOGY OF POST OPERATIVE NAUSEA AND VOMITING

I. Non Anaesthetic Factors

- Patient related factors
- Surgical factors

II Anaesthesia Related Factors

- Pre medication
- Gastric distension and suction
- Anaesthetic techniques and agents
- Post operative factors

Patient Related Factors

1. Age: Incidence in children increases after 3 yrs with a peak in 11 – 14 years age group and decreases in the elderly.[2]
2. Gender: Female patients have a 2 to 3 times greater incidence of post operative nausea and vomiting especially in ovulatory and luteal phase .[3,4]
3. History of motion sickness also increases the incidence due to lower threshold and a well developed reflex arc for vomiting.

4. Obesity: There is a positive correlation between body wt. and post operative nausea and vomiting and is due to the fact that adipose tissue acts as a reservoir for inhaled anesthetic agents and they are more prone for oesophageal reflux disease.[2,5]

5. Pre operative anxiety: It has been suggested that increased levels of catecholamines may be a contributing factor, excessive air swallowing seen in anxious patients, cause gastric distension resulting in vomiting.

Surgical factors

(i) Type of Surgery:

High incidence have been reported in Laparoscopic, Gynecological, breast surgeries, gallbladder, ENT, and Strabismus surgeries. Post operative nausea and vomiting after middle ear surgery increases upto 80%.[6]

(ii) Duration of surgery:

Longer durations allow longer exposure to lipid soluble, potentially emetic Intravenous/Inhalational anesthetics. This can trigger vomiting in the post operative. period.

ANAESTHESIA RELATED FACTORS

(i) Pre medication

Pre medication with opioids increase the incidence, by stimulating opioid receptors. Opoids pre dispose to post operative nausea and vomiting by sensitizing the otic and vestibular areas to motion They prolong gastric emptying time by decreasing gastric and GI motility, . However if opioids are not given it still causes vomiting due to increased pain. [2,7]

Benzodiazepam decreases the incidence of post operative nausea and vomiting by decreasing the plasma level of catecholamines. Atropine cause relaxation of the sphincter and delays gastric emptying.[8]

(ii) Gastric distension and suctioning:

Gastric suctioning may reduce post operative nausea and vomiting following difficult and vigorous mask ventilation, but the continued presence of NG tube, may stimulate the gag reflex.[2,7]

(iii)Anaesthetic Techniques And Agents

(a)Spinal anaesthesia is generally associated with less emesis than General Anaesthasia. Cephalad migration of opioids stimulate area postrema. This is common with less lipid soluble

agents like morphine. High blockade due to un opposed vagal tone increases GI peristalsis and cause vomiting

(b) Volatile Anaesthetics:

Due to sympathetic stimulation of older anaesthetic agents like ether, choloroform, and cyclopropane the incidence was higher than more recently introduced fluorinated anaesthetics. However newer agents also causes early post operative nausea and vomiting[10]

N_2O can cause post operative nausea and vomiting with a incidence ranging from 49-67% . It contributes through the following[7]

- Diffusion of N_2O into the middle ear increases its pressure and consequent stimulation of vestibular system.
- Gaseous distension of the bowel.
- Sympathetic stimulation.

However in one study by Muir et al found that there is no association between N_2O and development of post operative nausea and vomiting.

(c) Intravenous Anaesthetics

Ketamine and etomidate based anaesthesia cause more post operative nausea and vomiting than thiopentone and methohexitone. The emetic effects of ketamine may be due to release of endogenous catecholamines . [2]

Propofol and midazolam have been shown to be associated with less post operative nausea and vomiting.

Neostigmine used for reversal of muscle relaxation may increases post operative nausea and vomiting due to increased gut motility.[9]

(d) Postoperative Factors

(i) Pain: Visceral/Pelvic pain can cause post operative nausea and vomiting.

(ii) Ambulation:

Sudden movements, changing in posture can precipitate vomiting in patients receiving opioids.

(iii) Postural hypotension in post operative period can increase the incidence of post operative nausea and vomiting.

(iv) Opioids:

Nausea and Vomiting are common side effects of opioids administered during post operative period.

COMPLICATIONS OF POST OPERATIVE NAUSEA AND VOMITING

Patient related:

Post operative nausea and vomiting causes delay in ingestion of fluids, foods, oral medication and causes accompanying pain and discomfort.[2,7]

Medical:

post operative nausea and vomiting cause interruption of diet, nutrition, oral drug therapy, aspiration of gastric contents electrolyte imbalance, dehydration, Tachycardia, cardiac dysrrythmyias, increased intracranial tension, intraocular pressure and bloodpressure.[2,7]

Surgical:

Surgical complications include visceral wound dehiscence, bleeding at the surgical site, disruption of vascular grafts and anastamoses, and oesophageal rupture (or) tears.

Cost:

post operative nausea and vomiting cause increased stay in Hospital and cost and delay in returning to work.

Apfel et al concluded a prediction that female sex, history of motion sickness / post operative nausea and vomiting, non smoking status, use of post operative opioids were associated with increased incidence of post operative nausea and vomiting [11]. The incidence of post operative nausea and vomiting with 0,1,2,3, or all 4 of these risk factors were 10%, 21%, 39%, 61% and 79% respectively.

PERIOPERATIVE MANAGEMENT OF POST OPERATIVE NAUSEA AND VOMITING

Through pre operative assessment of patient if two or more risk factors are present, then appropriate modification may be made in the plan of anaesthesia such as avoidance of emetic agents (or) by giving prophylactic anti emetic therapy.

In addition to prophylactic anti emetic therapy other measures to decrease the incidence of post operative nausea and vomiting include:[12, 13]

- Minimizing gastric volume and distension by fasting,
- Addition of H2 receptor antagonist,
- Prokinetic agents,
- non particulate antacids to reduce PH,
- Administration of anxiolytic agents like midazolam,
- Avoidence of drugs like atropine that decrease sphincter tone ,
- Use of intravenous anaesthestics like propofol,
- Prevention of excessive stomach distension with mask ventilation by gastric suctioning,
- Maintenance of adequate fluid status intra operatively,
- Prevention of hypoxia, hypercarbia and hypotension ,
- Use of regional blockade whenever possible ,
- Minimize the usage of opioid analegic through use of NSAIDS

and local infiltration,

- Avoidence of early and excessive movement,
- Prompt removal of oral/ nasal tubes will all decrease post operative nausea and vomiting .

ANTI EMETIC THERAPY

1. **Pharmacological Therapy**
2. **Non Pharmacological Therapy**
3. **Adjuvant Therapy**

1. Pharmacological Therapy

Many of the concepts of anti emetic therapy in surgical populations have been adopted from successful treatment protocols utilized in oncology in relation to chemotherapy induce emeses.

Four major neurotransmitter systems appear to mediate the emetic response.

Dopaminergic (D2) histaminic (H1) cholinergic muscarinic and serotonergic.

Based upon the receptor sites traditional anti emetics that block the different neurotransmitter receptors are used.

The ideal anti emetic drug should be effective in preventing and treating nausea and vomiting with minimal side effects, it should be easy to administer and it should be long acting. In this regard no single anti emetic drug is 100% effective due to multifactorial stimulation for post operative nausea and vomiting and so a multi model approach is the best approach.

Anticholinergics:

They probably act by blocking conduction of nerve impulse across a cholinergic link through Muscarinic M_3 and M_5 receptors.

(e.g) Hyoscine (0.2 - 0.4 mg oral, Im) and dicyclomine (10 - 20mg oral)

uses: for the prophylaxis of motion sickness.

Main side effects are dry Mouth, sedation, blurred vision, memory loss, confusion and urinary retention.

Anti Histamines:

They act on the vomiting center, vestibular pathways with little action at the CTZ. They block acetyl choline receptors in vestibular apparatus and H1 receptors in the nucleus of solitary tract

Uses:Prophylaxis and therapy of vertigo, motion sickness and in control of emesis following middle ear surgery. They block the extra pyramidal side effects of metoclopramide.

(e.g): Promethazine Diphenhydramine, Dimenhydramine

Main side effect is excessive sedation.

Neuroleptics (Butyrophenones):

They are potent anti emetics, act by blocking D_2 receptor in CTZ and area postrema. They are more effective when given at the

end of surgery than at induction. Not effective in motion sickness because the vestibular pathway dose not involve dopaminergic link.

(e.g) Proclorperazine, Chlorpromazine.

Side effects: Drowsiness, extra pyramidal reactions.

Prokinetic drugs:

(a) Benzamides:

It is chemically related to procainamide and has both central and peripheral antiemetic actions. It acts through both dopaminergic and serotonergic pathways.

It blocks D_2 receptors and enhances acetylcholine release in GIT promoting gastric emptying and increases lower oesophageal tone. Central D_2 antagonism on CTZ is also responsible for its anti emetic activity. Because of its short duration of action it is not administered before induction.

Side Effects:

Sedation, dizziness, muscle dystonias. Long-term use causes parkinsonism and galactorrhoea.

(b) Domperidone:

It is a D_2 Antagonist, chemically related to haloperidol. Blocks D_2 receptors in upper GI. It crosses BBB poorly, so extra pyramidal side effects are rare. Well absorbed orally. Bio availability is only

15%.

Side Effects:

Dry mouth, loose stools, head ache, galactorrhoea.

(c) Phenothiazines:

They are widely used as anti emetics world wide. They exert a direct dopamine (D_2) receptor blocking effects on CTZ with moderate antihistaminic and anticholinergic actions.

They have an aliphatic (less anti emetic and less extra pyramidal) and heterocyclic (more extra pyramidal) ring compounds.

Neuroleptic malignant syndrome, dry mouth, urinary retention tachycardia are the main drawbacks of these drugs.

Other Adjuvants:

(I) Benzodiazepines:

They have weak anti emetic property based mainly on sedation. They alleviate the anxiety and there by decrease catecholamine levels and producing amnesia for the unpleasant procedures and hence reduce post operative nausea and vomiting.

(II) Clonidine:

The antiemetic effects of clonidine is multifactorial. They significantly reduce the volatile anaesthetic requirement, a general reduction in sympathetic out flow and the analgesic effect. All reducing the incidence of post operative nausea and vomiting [21]

(III) Ephedrine:

It is an indirectly acting sympathomimetic drug, which can prevent motion sickness and post operative nausea and vomiting secondary to fluid dehydration and orthostatic hypotension.[14]

(IV) Neurokinin Antagonists:

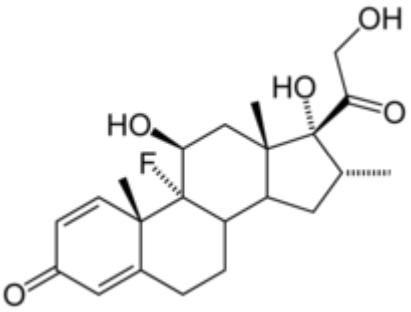
They are effective in the prevention of post operative nausea and vomiting because of their ability to block input from emetic stimuli in CNS. They act synergistically with $5HT_3$ antagonists.

Non Pharmacological Therapy:

Compared to placebo, acupuncture use in various forms effectively reduces post operative nausea and vomiting.

Most studies use P_6 (nei-guan) Pericardium point. It is recommended that stimulation be initiated before induction.[15]

DEXAMETHASONE



In 1980, Rich at al demonstrated the effectiveness of methyl prednisolone in controlling nausea and vomiting following cancer chemotherapy.[16] Later Dexamethasone was also reported as a useful anti emetic in chemotherapy induced nausea and vomiting[17]

Various randomized controlled study have shown that dexamethasone and other agents were effective in preventing nausea and vomiting.

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Mechanism of action :

The exact mechanism of dexamethasone induced anti emetic activity is not fully understood. It may involve two theories:

(1) Central inhibition of prostaglandin synthesis and release of

endorphins, resulting in mood elevation, a sense of well being and appetite stimulation.

(2) By depleting its precursor tryptophan.[19] They regulate neurotransmitter concentrations, receptor densities, signal transduction and neuronal configuration. [18]

Numerous glucocorticoid receptors are found in the nucleus of tractus solitarius, the raphe nucleus and area postrema.

Dexamethasone may have anti vertigo effect due to the anti inflammatory action, reducing the transient vestibulitis following surgical insult.

Dosage : 8 -20 mg intravenous

The plasma elimination half life of dexamethasone is approximately 4 to 4.5hrs and its duration of action is 36 to 72 hr.[18]

Side effects:

The most commonly reported adverse effects are flushing and perineal itching[20]

SEROTONIN ANTAGONISTS

Serotonin (or) 5-hydroxytryptamine, is a biogenic alkylamine synthesized from tryptophan. 90% of serotonin is located peripherally in the entero chromaffin cells of intestinal mucosa and 10% is found in CNS.

Serotonin receptors are found peripherally in the vagus nerve terminals and centrally within the limbic system, cerebral cortex and the chemoreceptor trigger zone.

Serotonin receptors have been categorized into five main subclasses. The majority of the receptors are G-protein-coupled receptors with the exception of $5HT_3$ receptor, which are ligand gated or fast ion channel.

All receptors are involved in physiologic functional response with the $5HT_3$ receptor being involved in the process of vomiting. The $5HT_3$ receptor was identified specifically as a target for anti emetics when fozard observed that metoclopramide had weak $5HT_3$ antagonistic properties.

The $5HT_3$ receptor antagonists are potent and highly selective competitive inhibitors of the $5HT_3$ receptor with a selectivity ratio of 100:1 for the $5HT_3$ receptor as compared to the other 5HT receptor.

The anti emetic action of the $5HT_3$ antagonists is due to simultaneous effects at both central and peripheral $5HT_3$ receptor sites.

$5HT_3$ receptor antagonists are rapidly absorbed and cross the

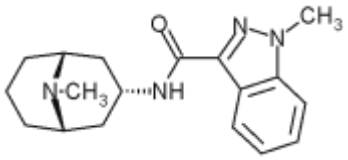
blood brain barrier, their elimination half life varies from 3 – 4 hrs for ondansetron and granisetron to 7 – 10 hrs. for Dolasetron. Overall the duration of anti emetic effect appears to be longer than what would be expected due to their increased affinity for the $5HT_3$ receptor site[22]

They are metabolized via various subtypes of cytochrome P–450 system in the liver and the resulting metabolites are excreted mainly in the urine.

By selectively working at the $5HT_3$ receptors, $5HT_3$ antagonists avoid the adverse effects of some of the traditional anti emetics.

They are tolerated over a wide dose range, most common side effects are headache and constipation

GRANISETRON



It is an Indazole derivative

It is a 5HT3 – receptor antagonist, which is 10-15 times more potent than ondansetron .

Formula: C18H24N4°

Mol.Weight: 312.4

Mechanism of action:

Cytotoxic drugs and radiotherapy produce nausea and vomiting by causing cellular damage → release of 5HT from intestinal mucosa → activation of vagal afferent gut → impulses to NTS and CTZ. Granisetron blocks emetogenic impulses both at their peripheral origin and central relay. Its main effect is to reduce the activity of the vagus nerve. It does not block dopamine receptors. The weak 5HT4 blockade action found with ondendetron is not detected.

Pharmacokinetic data:

Plasma half life : 3-14 hrs. But the anti emetic effect persists long after the drug disappears from the circulation, suggesting their continued interaction at the receptor level[23]

Volume of distribution: 3.07 L/kg

Peak plasma concentration :64 ng/min

Bioavailability : 60%

Protein binding : 65 ± 9%

Urinary excretion : 16 ± 14%

Faecal excretion : 38%

Clearance : 11 ± 9 ml/min/kg

Metabolism :

Its metabolism involves N-Demethylation amd aromatic ring oxidation followed by conjugation.

Therapeutics :

Available as injection, tablets & Syrup form

Dosage :

40mcg/kg.

To be reduced in aged, cirrhosis

No change in renal disease

Uses:

Post operative nausea & vomiting, chemotherapy induced vomiting.

Side Effects:

Constipation, headache, light headedness, induce minor ECG changes which are clinically insignificant

REVIEW OF LITERATURE

1. Fujii Y, Tanaka H, Toyookh [24] in a double blind study examined the useof granisetron Dexamethasone combination for the prevention of post operative nausea and vomiting (post operative nausea and vomiting) in female patients. For a period of 24 hrs, after surgery, a complete response (emesis free) was observed in 96% of patients who received granisetron plus dexamethasone and 82% on patients who received granisetron alone and 50% in placebo. No clinically important adverse events were observed in any group. Sub analysis based on the data shows granisetron plus dexamethasone is more effective than granisetron alone.

2. Fujii Y, saitoh y et al[25] did a randomized double blind study examining the effectiveness of granisetron 40mcg/kg , Dexamethasone 150mcgs/kg and granisetron 40mcg/kg plus Dexamethasone 150mcg/kg for the prevention of post operative nausea and vomiting in children. A complete response (no post operative nausea and vomiting) was 86% in granisetron 68% with dexamethasone and 98% with granisetron plus dexamethasone. They conclude that prophylactic therapy with combined granisetron and Dexamethasone was more effective.

3. Fujii Y, Toyooka H, Tanaka H [26] in another double blind study examined the efficacy of granisetron (40mcg/kg) Droperidol (20 mcg/kg) and metoclopramide 0.2 mg/kg in pt. undergoing middle ear surgery (The conclusion was prophylactic therapy with granisetron is superior in the prevention of post operative nausea and vomiting after middle ear surgery.

4. Fujii Y, et al[27] in a another study in patients undergoing Laparoscopic cholecystectomy, examined the effective dose of granisetron for the prevention of post operative nausea and vomiting. The incidence of post operative nausea and vomiting during the first 24hrs, was 43%, 40%, 13% and 13% after administration of saline, 20 mcg/kg, 40mcg/kg and 80mcg/kg of granisetron respectively. They concluded that granisetron 40mcg/kg is the minimum effective dose in the prevention of post operative nausea and vomiting.

5. Madan R, Bhatia A et a[28] in a double blind study evaluated the efficacy and safety of different doses of prophylactic intravenous dexamethasone for post operative nausea and vomiting and they concluded that dexamethasone 0.25mg/kg is the effective dose in preventing post operative nausea and vomiting.

6. Lee Y. Lai H y et al[29] evaluated the anti emetic effect of intravenous dexamethasone for post operative nausea and vomiting in women with and without H/o motion sickness and they concluded that prophylactic administration of dexamethasone is effective in reducing post operative nausea and vomiting in patients with and without H/o of motion sickness.

7. Fujii Y, Tanaka H[30] in a double blind study compared the efficacy of granisetron alone with granisetron plus dexamethasone for the treatment of nausea and vomiting after major gynecological surgery. In this study, they concluded that granisetron plus Dexamethasone was more effective than granisetron alone for the management of nausea and vomiting during 0-3hrs after major gynecologic surgery.

8. Matsuoka S, okamotos et al[31] in a prospective randomized study compared the efficacy and toxicity of granisetron and dexamethasone with those of granisetron alone for anti emetic control in patients receiving high dose chemotherapy with/without irradiation. They concluded that granisetron plus Dexamethasone seems superior to granisetron alone and they found more frequent side effects, but none of the events were serious.

9. Henz, I walder B et al [32] in a quantitative systematic review from 17 trials found that the best prophylaxis currently available for post operative nausea and vomiting is achieved by combining dexamethasone with a $5HT_3$ receptor antagonist.

10. AL pappar et al[33] examined the effectiveness of preoperative dexamethasone for post operative nausea and vomiting and 24 hrs recovery in children undergoing tonsillectomy. They concluded, that dexamethasone significantly decreased the incidence of post operative nausea and vomiting during the 24hrs after discharge.

11. Jhi-Joung wang et al[34] evaluated the timing effect of Dexamethasone for post operative nausea and vomiting in 120 patients and concluded that, the prophylactic intravenous administration immediately before the induction, rather than at the end of anesthesia was more effective in preventing post operative nausea and vomiting.

12. Al-shehri A m at el[35] in a double blind study found that inj. Dexamethasone therapy for post tonsillectomy patients significantly reduces nausea vomiting and pain and had better out come.

13. Fujii Y, Tanaka H et al[36] in a study concluded that Dexamethasone 8 mg enhances the anti emetic efficacy of granisetron but dose not potentiate the other anti emetics droperidol and metoclopramide in female patients undergoing major gynecological surgery.

14. D' Angelo R et al[37] in a pilot study explore the dose – response relationship between granisetron administered and post operative nausea and vomiting symptoms. They concluded a trend of improved efficacy with dose of 0.1, 0.2, 0.3 mg. This study did not identify a dose response relationship.

15. Biswas BN et al[38] concluded the combination (Granisetron plus Dexamethasone) increases the chance of complete response than granisetron alone. So the combination might be considered clinically relevant in a high risk setting.

16. De wit R. et a[39] concluded a study of cross over to granisetron after failure to ondansetron plus dexamethasone following highly emetogenic chemotherapy. They concluded that patients who have acute protection failure on one 5HT3 receptor antagonist (ondansetron) should be offered to cross over another (Granisetron).

17. Fujii Y at al[40] in a study to determine the minimum effective dose of granisetron for the prevention of post operative nausea and vomiting after middle ear surgery. They conclude Granisetron 40 mcg/kg appears to be the minimum effective dose for preventing post operative nausea and vomiting in women undergoing middle ear surgery.

MATERIALS & METHODS

After obtaining approval from our institutional ethics committee and informed consent, 90 Patients of (ASA Physical status 1) aged 15 - 50 yrs. with body weight ranging 40 – 80kgs. scheduled for elective ENT surgeries were studied at the **Govt. Stanley Hospital, Chennai**.

Patient with cardiovascular, respiratory, renal or hepatic diseases, pregnant, lactating (or) menstruating women and those taking medications which would affect the study, those who had a H/o of motion sickness and or previous H/o of post operative nausea and vomiting were excluded from the study.

Premedication - Intramuscularly Pentazocine 0.5 mg/kg, Glycopyrolate 0.2mg half an hour before surgery for all patients.

Patients were randomly allocated into three different groups (30 in each group). Patients were given in a randomized, double -blind manner, a single dose of normal saline (placebo) 5ml, (or) Inj.Granisetron 40mcg/kg,(GROUP –II) (or) Inj. Granisetron 40mcg/kg with dexamethasone 8mg, (GROUP –III) intravenously. Study medications were prepared by personnel not involved in the study in identical 5 ml volume. The study drugs were given just after intravenous cannulation ,

before Induction of anaesthesia.

The patients were fasted for eight hours before surgery and on arrival to the operating theatre, routine monitoring devices were attached and basal HR, BP, ECG, SPO_2 were observed and also observed throughout the study period.

Anaesthesia was induced with Thiopentone 5 mg/kg intravenously and succinylcholine 2mg/kg intravenously was used to facilitate tracheal intubation.

After tracheal intubation, anaesthesia was maintained with 66% nitrous oxide,33%oxygen with 0.5% halathone with pancuronium bromide as non depolarising muscle relaxant.Ventilation was controlled mechanically in all patients.

At the completion of surgery, residual neuro muscular blockade was antagonized with intravenous Glycopyrolate 0.01mg/kg and neostigmine 0.04mg/kg. the trachea was extubated when the patient was awake. Patients were shifted to the recovery room.

They were asked to inform whether they had nausea, retching (or) vomiting during the first 24 hrs and was recorded . The results

were scored in a manner similar to **Belville et al.**

Grade 0 - No nausea /retching / vomiting

Grade 1 - Nausea/retching

Grade 2 - Vomiting

Patients were assessed for nausea, retching and vomiting at 1,2,4,12 & 24 hrs post operatively. If two (or) more episodes of emesis occurred Inj. Metoclopramide 10mg iv. as rescue antiemetic was given.

Results were statistically analysed with t test, chi – square test

They were also enquired about adverse effects like Headache, sedation, abdominal discomfort, dizziness etc and noted.

Group wise comparison of the baseline characteristics

TABLE – I

Parameter	Group I (N = 30)	Group II (N = 30)	Group III (N = 30)	P value	Inference
Age (Years)	29.2 ± 8.04	29.8 ± 9.7	29.1 ± 9.8	0.951	NS
Weight (Kg)	56.3 ± 6.9	59.3 ± 9.89	61.23 ± 10.26	0.1188	NS
Sex (M:F)	14 ± 16	19 ± 15	16 ± 14	0.875	NS

P>0.05 indicates statistically not significant

TABLE – II

Parameter	Group I (N = 30)	Group II (N = 30)	Group III (N = 30)	P value	Inference
BP Systolic	122.4 ± 7.9	119.5 ±9.38	121.6 ±10.12	0.4598	NS
BP Diastolic	79 ± 7.12	77.4 ± 8.2	76.4 ± 6.8	0.396	NS
Surgical Duration(mins)	96.7 ± 20.5	93.67 ±19.8	94.17 ± 18.9	0.817	NS
Pulse Rate	82 ± 4.90	82.2 ± 6.8	79.8 ± 5.1	0.208	NS

P>0.05 indicates stastically not significant .

Table III (a)

Incidence of Nausea according to Groups

Table III (b)

Comparison of Nausea	P Value	Inference
Group I vs Group II	< 0.001	S
Group I vs Group III	<0.001	S
Group II vs Group III	<0.02	S

Incidence of Retching according to Groups (0-24 hrs)

Table - IV

Retching	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
Presence	24	80	5	16.7	1	3.3
Absence	6	20	25	83.3	29	96.7
Total	30	100	30	100	30	100

P value <0.001

Incidence of Vomiting according to Groups (0-24 hrs)

Vomiting	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
Presence	24	80	6	20	1	3.3
Absence	6	20	24	80	29	96.7
Total	30	100	30	100	30	100

P value <0.001

Comparison of Vomiting

Comparison of Vomiting	P Value	Inference
Group I vs Group II	< 0.001	S
Group I vs Group III	<0.001	S

Group II vs Group III	<0.05	S

TABLE V(b)

Distribution of Incidence of Vomiting according to Groups

Vomiting episodes	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
None	6	20	24	80	29	96.7
Single	6	20	3	10	1	3.3
Multiple	18	60	3	10	0	
Total	30	100	30	100	30	100

Distribution of Patients according to Nausea score

Grade 0	Grade 1	Grade 2
No Nausea/Vomiting	Nausea/Retching	Vomiting
No Rescues		

TABLE V (c)

Grade	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
0	3	10	23	76.7	29	96.7
1	3	10	1	3.3	0	
2	24	80	6	20	1	3.3
Total	30	100	30	100	30	100

TABLE -VI

Group wise distribution of side effects

Side effects	Group I		Group II		Group III		P Value
	No.	%	No.		%	No.	%
Headache	3	10	3	10	2	6.7	0.87
Sedation	1	3.3	1	3.3	2	6.7	0.76
Abdominal discomfort	1	3.3	1	3.3	1	3.3	1
Dizziness	2	6.7	1	6.7	2	6.7	0.80

RESULTS

This was a randomised, double blind placebo controlled study conducted at Govt. Stanley Hospital. CHENNAI AFTER OBTAINING INFORMED CONSENT FROM ALL THE 90 PATIENTS SUBJECTED TO STUDY. They were grouped into three groups and received placebo, Granisetron 40 mcg's/Kg and Granisetron 40 mcg'/kg with dexamethasone 8 mg.

Age, weight, sex distribution, systolic & Diastolic Blood pressure, Heart rate were not significantly different in these groups as can be seen in table I. and table II.

Surgical duration :

Group I	Group II	Group III
96 + 7 ± 20.53	93.67 ± 19.87	94.17 ± 18.94

Incidence & Severity of Nausea

Table III (a) shows incidence of nausea 0- 24 hrs. As shown in Table III (a) 90% of the patients in the group I and 23% in the group II had nausea while it fell to 4% in group III.

Comparison of Nausea between Groups

Table III b compares the incidence of nausea between each groups individually ie. Group I with Group II and Group II with Group III. etc.

From the above mentioned table one we see that , the incidence of nausea is reduced significantly both in Group II and Group III .Among these two, the grade 0 was in 96% of patients in Group III ($P<0.05$).

Incidence of Retching

Similarly the incidence of retching was compared in all the three groups. Group I shows an incidence of 80% and group II shows 17% and group III shows only 4%.

Incidence of Vomiting

As seen in table V (a) the Incidence of vomiting in group I is 80% and in group II it is 20% and in group III is only 4%.

When number of episodes are compared as shown in table V (b), it was seen that in group I it is 60%, in group II it is10% and none in group III have multiple episodes and the need for rescue antiemetic.

Comparison of Vomiting between Groups

Table V (b) statistically analyses the differences in the incidence of vomiting when compared with group I , group II shows statistically significant but Group III is more effective.

Table V(c), shows a complete response (no post operative nausea and vomiting) occurred 96% in group III and 77% in group II and 10% in group I . Thus a complete response was significantly more common in the patients who had received the drugs Granisetron and Dexamethasone.

Table VI shows the Incidence of some side effects which were not statistically significantly among the groups.

DISCUSSION

Post Operative Nausea and Vomiting is distressing and sometimes, the patients dread it more than post operative pain. There are various factors that predispose a Patient to post operative nausea and vomiting. It is more frequent in women, in non smokers, in Pts with a past History of motion sickness, morning sickness or post operative nausea and vomiting and with perioperative use of opioid.

The frequency of nausea and vomiting following middle ear surgery can be as high as 62%-80%. If the prophylactic anti emetic is not given in our study the incidence is little bit higher of about 90% in control group.

Prophylactic administration of scopolamine, prochlorperazine, droperidol, $5HT_3$ antagonists and combination of anti emetics have been advocated for post operative nausea and vomiting in middle ear surgery and in ENT surgeries in various studies. Ondansetron has been less effective in preventing post operative nausea and vomiting in middle ear surgery patients.[41]

Granisetron alone (or) in combination with dexamethasone has been shown to be highly effective in patients undergoing middle ear surgery as concluded by Fujii et al in various studies.[24,25,13]

In high risk population, the current mode of preventing post operative nausea and vomiting is by multimodal therapy and commonly used combinations are $5HT_3$ receptor antagonist & Dexamethasone.[13]

So in our present study we tried to compare the efficacy of Granisetron 40 mcg/kg with Granisetron 40 mcg/kg plus Dexamethasone 8mg and found statistically significant decrease in the incidence of nausea and vomiting between group I , group II and Group III.

All factors which predisposed to increase post operative nausea and vomiting like age,obesity, gender, durations type of surgery, anaesthetic technique are equally distributed among the groups and hence the difference in the incidence of complete response between groups and the requirement of rescue anti emetics between groups can be attributed to the difference in the anti emetics tested.

The possible mechanism of Dexamethasone action might be to decrease the level of prostaglandins in the central nervous system.

They regulate neurotransmitter concentrations, receptor densities signal transduction and neuronal configuration. [19,13]

As concluded in many studies the granisetron plus Dexamethasone significantly reduces the post operative nausea and vomiting when given prophylactically.[24,25,38]It is usually recommended that an anti emetic be given prophylactically before surgery or chemotherapy to improve the efficacy of the drug. Hence, the study agents were administered intravenously before the commencement of surgery. The dose of granisetron used in this study was based on the previous studies by Fujii et al.[27] They have suggested that 40 mcg/kg was the minimum effective dose for prevention of post operative nausea and vomiting following surgery. The dose of dexamethasone used (8 mg)[28] was based on the studies previously shown to decrease emesis when added as an anti emetic regimen. In the present study, therefore, the same dose of dexamethasone was added to granisetron.

The precise mechanism by which dexamethasone increase the effectiveness of granisetron is not known. Granisetron produces antiemesis by blocking $5HT_3$ receptors. Dexamethasone may inhibit stimulation of $5HT_3$ receptors and may also potentiate the other pharmacological receptors[32,28]

Ali sz et al studied the effects of pre-op fluid[12] on the post operative nausea and vomiting and found a considerable decrease in the incidence of post operative nausea and vomiting.

Apfel cc et al concluded that volatile anaesthetics[10] were the leading cause of early post operative vomiting. The pro emetic effect was larger than other risk factor. In patients who are at high risk for post operative nausea and vomiting, it would therefore be better to avoid inhalation anaesthesia.

Adeno -tonsillectomy is also associated with a high post operative nausea and vomiting rate (36-76%) patel R. Rouley. This is thought to be due to the irritant effects of blood on oesophago gastric chemo receptors, irritation of trigeminal afferents during surgery.

In our study the incidence of post operative nausea and vomiting is high among female patients.

Obesity increases the incidence of vomiting, in our study patients who weighed more than 60 kg had increased incidence. Gigilo at al [41] in their study to prevent nausea and vomiting following cancer chemotherapy concluded that both ondansetron and granisetron have similar anti emetic efficacy but dose of granisetron is much less than

ondansetron iv. Moreover ondansetron has a shorter half-life of 3 hrs, whereas granisetron has a half life of 8-9 hrs, for for which it is more effective in preventing nausea and vomiting. Granisetron is also a more selective 5HT3 receptor antagonist than ondansetron[44,42]

In our study the need for rescue antiemetic in group I is 60%, groupII is 10% where as in group III is nil.

The safety of intravenous and oral granisetron has been evaluated in more than 7,000 patients in clinical trial, which have shown the drug to be well tolerated, with mild and transient side effects. There have been no reports of extrapyramidal side effects with either intravenous or oral granisetron for the prevention and treatment of chemotherapy-induced emesis and post operative nausea and vomiting. In our study also patients tolerate the drug well with few side effects .

In our study patients receiving placebo had stayed in the hospital more than patients receiving Granisetron with dexamethasone.

CONCLUSION

Antiemetic prophylactic should be definitely included in the anaesthetic management of patients with risk post operative nausea and vomiting undergoing general anaesthesia.

Granisetron is effective in preventing post operative nausea and vomiting in majority patients.

Granisetron plus Dexamethasone combination prophylaxis is highly effective in controlling postoperative nausea and vomiting with few side effects.

BIBLIOGRAPHY

1. Watcha M F, White P F. Post operative nausea vomiting; do they matter? Eur J Anaes 1995 may 10;18-23

2. Watcha M F, White P F. Post operative nausea vomiting ;its etiology, treatment and prevention. Anaesthesiology 1992; 77; 162-84

3. Honkovara P, Nausea and vomiting after gynecological laparoscopy depends upon the phase of menstrual cycle Canad. J. of anaes;38:376

4. Beattic W S, the incidence of PONV in woman undergoing laparoscopy is influenced by the day of menstrual cycle Cand. J. of anaes; 1991;38:298

5. Kenny G.N.C. risk factors for PONV , Anaesthesia: 1994; 49(suppl):6-10

6. Honkovara P, Saarinvaara L. Prevention of nausea, vomiting with transdermal hyocine in adults after middle ear surgery

7. Kovac AL, PREVENTION OF ponv. Drugs 2000;59:213-243.

8. Splinter WM, Mac Neil HB,Menard EA, Rhine EJ Midazolam reduces vomiting after tonsillectomy in children Cand.J.Anaes 1995;41:201-203.

9. Boeke AJ,Effect of antagonizing residual neuromuscular block by neostigmine and atropine on PONV. Br.J.Anaes;1994;72:654-6.

10. Apfel CC, Kranke P,Katz MH,Goefer et al,Volatile anaesthetics may be the leading cause of early PONV. Br.J.Anaes 2003 jun ;

90(6)725-7

11. Apfel CC, Laara E, Katz mh,Greim LA, Roewern, A simplified risk score for predicting PONV, conclusions from cross validations between two centers. Anaesthesiology 1999;91:693-700

12. Ali SZ, Taguchi A, Holtmann B, Kurz A, Effevt of supplemental pre- operative fluid on PONV Anaesthesia;2003;aug 58:780-4.

13. Post operative nausea vomiting a reviw article; Indian Journal Anaesthesiology 2004;48(4)253-58.

14. Rothen berg DM et al. Efficacy of ephedrine in the prevention of PONV .Anaesth & Analg 1991;72:58-61.

15. Dandee JW. Effect of stimulation of P6 anti emetic point of PONV Br.J.Anaes 1984:63;612

16. Rich WM, Abdul hayoglya methyl prednisolone as an anti emetic drug during cancer chemo therapy a pilot study Gynecol oncol 1980;9:193-198.

17. Aapro MS,Albert DS.Dexamethasone as an anti emetic in patients treated with cis platin N.Engl.J.Med 1981;305:520.

18. Goodman and Gillman"s The Pharmacological Basis of Therapeutics 9th edition 1459-1486.

19. Henzi I, Walder B, Tramer MR.Dexamethasone for PONV.Anaesth & Analg 2000; 90: 186-194.

20. Thomas R,Jones N. Dexamethasone decreases nausea and vomiting after laparoscopy. Br.J.Anaes 2000; 85: 328-9

21. Mikawa K et al. Oral clonidine Premedication reduces vomiting

in children after strabismus surgery Can. J.Anaes 1995;42: 977-81.

22. Andrews PFR, Bhandari P, Davey PT, Binghar S et al. Are all 5HT3 receptor antagonist the same? Eur J Cancer 1992;28A:52-56.

23. Katzung. Bertram G. Basics and Clinical Pharmacology 9th edition(2004).

24. Fujii Y, Tanaka H, Toyooka H. Prophylactic anti emetic therpy with granisetron and dexamethasone combination in patients undergoing breast surgery ACTA Anaes Scand; 1998 Oct;42(9)1038-42.

25. Fujii Y, Saitoh Y Tanaka H,. Prophylactic anti emetic therpy with combined granisetron and dexamethasone for PONV in children. Eur J Anaes 1999 Jun; 16(6):376-9.

26. Fujii Y, Tanaka H, Toyooka H. Prophylactic anti emetic therpy with granisetron, droperidol and metoclopramide in patients under going middle ear surgery. Anaesthesia 1998:Dec;53(12):1165-8.

27. Fujii Y, Saitoh Y , Tanaka H, Toyooka H. Effective dose of granisetron for the prevention of PONV in patients undergoing laparoscopic cholecystectomy,Eur J. Anaes 1998;May 15(3) 287-91.

28. Madan R, Bhatia A, Chakithandy S, Subramanian R, Rammohan G et al. Prophylactic dexamethasone for PONV in pediatric strabismus surgery; a dose ranging and safety evaluation study . Anaesth & Analg 2005 Jun;100(6) 1622-6

29. Lee y, Lai HY,Lir PC, et al, Dexamethasone prevents PONV more effectively in women with motion sicknecc Can J Anaes 2003 Mar 50(3):232-7.

30. Fujii Y, Tanaka H, Granisetron versus granisetron with dexamethasone combination for the treatment of nausea, retching and vomiting after major gynecological surgery. Clinc Therap 2003 Feb; 25(2):507-14.

31. Matsuoka S, Okamoto S, et al. , Granisetron versus granisetron with dexamethasone combination in the prevention of vomiting induced by conditioning for stem cell transplantation; Int J Hematol. 2003 Jan;77(1) 86-90.

32. Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of post operative nausea vomiting: a quantitative review,. Anaesth Analg 2000 Jan; 186-94.

33. AL Pappas, R Sukhani, AJ Hotaling, et al. The effect of preoperative dexamethasone on the immediate and delayed postoperative morbidity in children undergoing adenotonsillectomy. Anaesth Analg 1998 vol 87, 57-61.

34. Jhi-joung wang, Shung- Tai ho, et al. The effect of timing of dexamethasone administration on its efficacy as a prophylactic antiemetic for PONV. Anaesth Analg 2000; 91: 136-139.

36. Fujii Y, Tanaka H, Toyooka H. The effects of dexamathasone on antiemetics in female patients undergoing gynecological surgey. Anaesth Analg 1997 Oct; 85(4): 913-7.

37. D' Angelo R, Philip B, Gan T J, Kovac A et al. A randomized, double- blind, close ranging, pilot study of intravenous granisetron in the prevention of PONV in patients undergoing abdominal hysterectomy. Eur J Anaesth. 2005 Oct ; 22(10): 774-9.

38. Biswas B N, Rudra A. Comparison of granisetron and granisetron plus dexamethasone for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. Acta Anaesthesiol Scand. 2003 Jan; 47 (1): 79-83.

39. de Wit R, de Boer A C, v d Linden GH, et al. Effective cross - over to granisetron after failure to ondensetron, a randomized double blind study in patients failing ondensetron plus dexamethasone during the first 24 hours following highly emetogenic chemotherapy. Br J Cancer, 2002 May 20; 86(10):1662-3; author reply 1664.

40. Fujii Y, Tanaka H, Toyooka H Granisetron in the prevention of nausea and vomiting after middle ear surgery: a dose- ranging study.Br J Anaesth, 1998 Jun;80(6):764-6.

41. Gigillo C A, Soares H,Castro C P et al Granisetron is equivalent to ondensetron for prophylaxisis of chemotherapy induced nausea and vomiting. Results of a meta analysis of randomized controlled trials. Cancer 2000 ; 89 : 2301 -8.

42. R Janknegt et al. Clinical efficacy of antiemetics following surgery. Anaesthesia 1999 ; 54 : 1059 – 68.

44. 43. Robert K Stoelting. Physiology and pharmacology for anaesthesia 3rd edition, page 406 – 7

A - Tonsillectomy

B - Myringo plasty

C - Tympano plasty

D - Stapedectomy

E - Septoplasty

F - FESS

PROFORMA

SI.No. ..... Name:..... Age/Sex:.....

IP.No.:..... Wt. :..... ASA :.....

Diagnosis:..... Surgery:.....

Study drug given before induction of Anaesthesia

Duration of Surgery: ……
(in mins)

	Pulse Rate	Blood Pressure
Pre OP :		
Intra OP :		
Post OP :		

Time in hours	1	2	4	12	24
Incidence of Nausea					
Retching					
Vomiting (no of episodes)					
Rescue antiemetic					

Side effects (if any) :